Remarks

None of the amendments add new matter. The amendments merely correct a formal matter without changing the scope of the claims.

The Examiner requested on May 22, 2003, that Fig. 1 on page 20 be deleted and, *in lieu* thereof, inserted at the end of the application. Further, the Examiner requested a new paragraph be added, entitled "Brief Description of the Drawings".

Accordingly, the application has been amended by inserting a sheet of FIGS. 1A-1D at the end of the application that correspond to the original Fig. 1. The symbols A, B, D, and D in the drawing have been amended to read FIG. 1A, FIG. 1B, FIG. 1C, and FIG. 1D, respectively. No new matter has been added by this amendment.

The specification has been amended by inserting a new paragraph entitled "BRIEF DESCRIPTION OF THE DRAWINGS" after paragraph [0019]. This new paragraph includes the first sentence of paragraph [0104] and the figure text below the Fig. 1. The symbols A, B, D, and D of the figure text have been amended to read FIG. 1A, FIG. 1B, FIG. 1C, and FIG. 1D, respectively. No new matter has been added by this amendment.

The specification has been also amended by deleting Fig. 1 and the figure text from paragraph [0104] at page 20. Further, paragraph [0104] has been amended by adding --A, B, C, and D-- after "protocols" at line 1 of the paragraph and replacing "(Fig. 1)" with --(FIGS. 1A-1D)--. No new matter has been added by these amendments.

Support for the amendments can be found in the original specification as filed. Accordingly, Applicants request that these amendments be entered.

Reconsideration of this application and entry of the above Amendment is respectfully requested.

Respectfully submitted,

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John M. Covert
Attorney for Applicants
Registration No. 38,759

Date: May 27, 2003

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137,025v1<SKGF_DC1>

Version with markings to show changes made

In the Application:

The attached sheet of FIG. 1A, FIG. 1B, FIG. 1C, and FIG. 1D has been inserted at the end of the application.

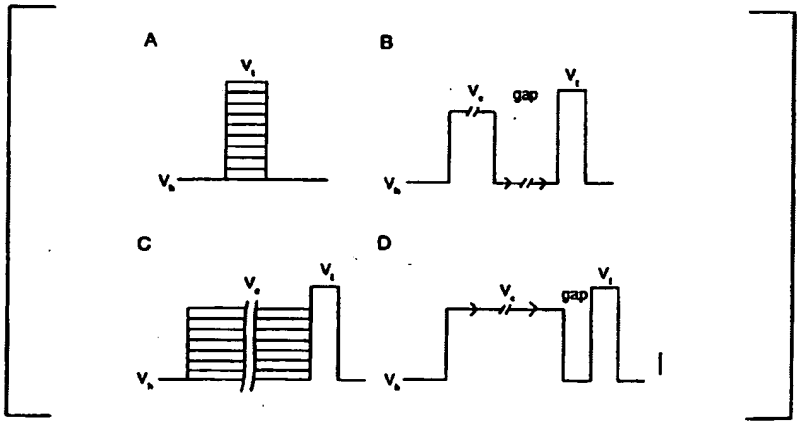
In the Specification:

A heading has been inserted after paragraph [0019] and above the heading "DETAILED DESCRIPTION OF THE INVENTION".

A new paragraph has been inserted under the heading "BRIEF DESCRIPTION OF THE DRAWINGS".

Paragraph [0104] at page 20 has been amended as follows:

The following voltage pulse protocols A, B, C, and D are used to assess the potency and kinetics of inhibition of the Na^+ channels by the compounds ([Fig. 1] FIGS. 1A-1D).



[Figure 1. Voltage pulse protocols. A. IV-curves. C. Steady-state inactivation. B. Repriming kinetics. D. Time course of binding.]

Current-voltage relationship (IV-curve), protocol **A**, is used to report the voltage at which the maximal inward Na^+ current is achieved. This voltage is used throughout the experiment as testing voltage, V_t. The steady-state inactivation (or, availability) curve, protocol **C**, is used to get the voltage at which almost complete (≥95%) inactivation of Na^+ channels occurs; it serves as voltage for conditioning prepulse, V_c, throughout the experiment. Protocol **B** reports how fast the channels recover from inactivation at hyperpolarized voltages. This permits us to set up the duration of the hyperpolarization gap which is used in measurement of the kinetics of binding of compounds to inactivated Na^+ channels (protocol **D**). Channel repriming under control conditions is fast (≥90% recovery during first 5-10 ms). If a drug substantially retards the repriming process, then it becomes possible (protocol **D**) to accurately measure the kinetics of binding of the inhibitor to inactivated channels as well as the steady-state affinity (k_+ and K_i). To estimate k_+ values, the reduction in peak currents in successive trials with varying pre-pulse duration is plotted as a function of pre-pulse duration and the time constant (τ) measured by mono-exponential fit. A plot of $1/\tau$ as a function of antagonist concentration then allows calculating of the macroscopic binding rates of the antagonists. To determine K_i values the partial inhibition curves measured by fractional responses in steady-state are fitted with the logistic equation:

$$I/I_{control} = 1/(1 + ([antagonist]/K_i)^p), \qquad \text{Eq. 2}$$

where $I_{control}$ is the maximal Na^+ current in the absence of antagonist, [antagonist] is the drug concentration, K_i is the concentration of antagonist that produces half maximal inhibition, and p is the slope factor.

		Due Date:	**June 13, 2003**
Applicants:	Hogenkamp *et al.*	**Art Unit:**	1626
		Examiner:	Shameem, G.
Application No.:	09/814,123	**Docket:**	1861.1270001
Filed:	March 22, 2001	**Atty:**	JMC/THN
For:	**Aryl Substituted Pyrazoles, Triazoles and Tetrazoles, and the Use Thereof**		

When receipt stamp is placed hereon, the USPTO acknowledges receipt of the following documents:

1. SKGF Cover Letter;
2. Amendment Under 37 C.F.R. § 1.312;
3. One sheet of drawings (Figs. 1A-1D); and
4. One (1) return postcard.

May 27, 2003

Via Hand Carry
Group Art Unit 1626
Examiner G. Shameem

SKGF_DC1:137223.1

Please Date Stamp And Return To Our Courier

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